



Clinical trial results:

A Phase 1b, Open-label study to Evaluate the PK, Safety and Efficacy of B/F/TAF in HIV-1 infected, Virologically Suppressed, Pregnant Women in their Second and Third Trimesters

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2021-001073-23 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 18 August 2022 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 29 December 2023 |
| First version publication date | 02 March 2023 |
| Version creation reason | <ul style="list-style-type: none">• New data added to full data setAdded neonates arm group in adverse events section. |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-380-5310 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03960645 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Gilead Sciences |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404 |
| Public contact | Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com |
| Scientific contact | Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com |

Notes:

Paediatric regulatory details

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|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 18 August 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 July 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 August 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the steady state pharmacokinetics (PK) of bicitgravir (BIC) and confirm the dose of BIC/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg fixed dose combination (FDC) in human immunodeficiency virus 1 (HIV-1) infected, virologically suppressed pregnant women in their second and third trimesters.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

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|---|--------------|
| Actual start date of recruitment | 28 June 2019 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Dominican Republic: 6 |
| Country: Number of subjects enrolled | Thailand: 49 |
| Country: Number of subjects enrolled | United States: 7 |
| Worldwide total number of subjects | 62 |
| EEA total number of subjects | 0 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 29 |
| Infants and toddlers (28 days-23 | 0 |

| | |
|---------------------------|----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 33 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the Dominican Republic, Thailand, and the United States.

Pre-assignment

Screening details:

33 pregnant women were enrolled in the B/F/TAF group. Neonates born to these women were also enrolled in the study for follow up. A total of 29 neonate participants were enrolled.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | B/F/TAF |

Arm description:

Pregnant women participants received fixed dose combination (FDC) tablet of bicitgravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg, orally, once daily for up to 38 weeks (from the second or third trimesters of pregnancy, depending on enrollment, through 12 weeks post-partum).

| | |
|--|-------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | B/F/TAF |
| Investigational medicinal product code | |
| Other name | GS-9883/F/TAF, Biktarvy®, BVY |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

50/200/25 mg FDC administered as a single dose.

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|------------------|----------|
| Arm title | Neonates |
|------------------|----------|

Arm description:

Neonates born to women participants in the study were followed from birth up to 8 weeks of age after obtaining consent from the parent or legal guardian. None of the neonates participating in the study were treated with the study drug.

| | |
|---|-----------------|
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 1 | B/F/TAF | Neonates |
|--------------------------------|---------|----------|
| Started | 33 | 29 |
| Completed | 32 | 29 |
| Not completed | 1 | 0 |
| Protocol Violation | 1 | - |

Baseline characteristics

Reporting groups

| | |
|--|----------|
| Reporting group title | B/F/TAF |
| Reporting group description: | |
| Pregnant women participants received fixed dose combination (FDC) tablet of bicitgravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg, orally, once daily for up to 38 weeks (from the second or third trimesters of pregnancy, depending on enrollment, through 12 weeks post-partum). | |
| Reporting group title | Neonates |
| Reporting group description: | |
| Neonates born to women participants in the study were followed from birth up to 8 weeks of age after obtaining consent from the parent or legal guardian. None of the neonates participating in the study were treated with the study drug. | |

| Reporting group values | B/F/TAF | Neonates | Total |
|---------------------------------------|---------|----------|-------|
| Number of subjects | 33 | 29 | 62 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years | | | |
| arithmetic mean | 30 | 0 | - |
| standard deviation | ± 5.0 | ± 0.0 | |
| Gender categorical Units: Subjects | | | |
| Female | 33 | 10 | 43 |
| Male | 0 | 19 | 19 |
| Race Units: Subjects | | | |
| Asian | 25 | 24 | 49 |
| Black | 6 | 4 | 10 |
| Other | 1 | 1 | 2 |
| White | 1 | 0 | 1 |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 4 | 4 | 8 |
| Not Hispanic or Latino | 29 | 25 | 54 |

End points

End points reporting groups

| | |
|--|----------|
| Reporting group title | B/F/TAF |
| Reporting group description: Pregnant women participants received fixed dose combination (FDC) tablet of bicitgravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg, orally, once daily for up to 38 weeks (from the second or third trimesters of pregnancy, depending on enrollment, through 12 weeks post-partum). | |
| Reporting group title | Neonates |
| Reporting group description: Neonates born to women participants in the study were followed from birth up to 8 weeks of age after obtaining consent from the parent or legal guardian. None of the neonates participating in the study were treated with the study drug. | |

Primary: Pharmacokinetic (PK) Parameter: AUCtau of Bicitgravir (BIC)

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|--|---|
| End point title | Pharmacokinetic (PK) Parameter: AUCtau of Bicitgravir |
| End point description: AUCtau is defined as concentration of drug over time (the area under the concentration verses time curve over the dosing interval). PK analysis set included all enrolled adult participants who took at least 1 dose of study drug (B/F/TAF), and had at least 1 non-missing concentration value reported by the PK laboratory for the corresponding analytes (BIC, FTC, TAF, and tenofovir diphosphate [TFV-DP]). Participants in the PK analysis set with available data were analysed. | |
| End point type | Primary |
| End point timeframe: Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The statistical analysis of this primary endpoint is provided in the attachment.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The neonates did not receive the study drug so they were not analyzed for the primary endpoint.

| End point values | B/F/TAF | | | |
|---|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: hours*nanograms per milliliter (h*ng/mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Second Trimester (n=20) | 62772.2 (± 20242.18) | | | |
| Third Trimester (n=30) | 60163.4 (± 17482.06) | | | |
| Week 6 Post-partum (n=31) | 134820.3 (± 36217.30) | | | |
| Week 12 Post-partum (n=32) | 148251.6 (± 42189.17) | | | |

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|-----------------------------------|---|
| Attachments (see zip file) | Statistical Analysis/380-5310_Primary_Endpoint_StatsAnalysis. |
|-----------------------------------|---|

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUCtau of Emtricitabine (FTC) and Tenofovir Alafenamide (TAF)

| | |
|-----------------|--|
| End point title | PK Parameter: AUCtau of Emtricitabine (FTC) and Tenofovir Alafenamide (TAF) ^[3] |
|-----------------|--|

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration versus time curve over the dosing interval). Participants in the PK analysis set with available data were analysed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

| End point values | B/F/TAF | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: h*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| FTC: Second Trimester (n=21) | 10263.8 (± 2054.35) | | | |
| FTC: Third Trimester (n=30) | 10435.2 (± 2121.87) | | | |
| FTC: Week 6 Post-partum (n=31) | 16277.5 (± 4023.42) | | | |
| FTC: Week 12 Post-partum (n=32) | 15308.5 (± 3359.83) | | | |
| TAF: Second Trimester (n=15) | 235.5 (± 107.36) | | | |
| TAF: Third Trimester (n=17) | 212.1 (± 95.38) | | | |
| TAF: Week 6 Post-partum (n=27) | 374.3 (± 153.54) | | | |
| TAF: Week 12 Post-partum (n=30) | 296.4 (± 94.37) | | | |

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| Attachments (see zip file) | Statistical Analysis/380- |
|-----------------------------------|---------------------------|

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUClast of BIC, FTC, and TAF

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|-----------------|---|
| End point title | PK Parameter: AUClast of BIC, FTC, and TAF ^[4] |
|-----------------|---|

End point description:

AUClast is defined as the concentration of drug from time zero to the last observable concentration. Participants in the PK analysis set with available data were analysed.

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| End point type | Secondary |
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End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

| End point values | B/F/TAF | | | |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: h*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| BIC: Second Trimester (n=21) | 63187.5 (± 19814.99) | | | |
| BIC: Third Trimester (n=30) | 60145.3 (± 17484.52) | | | |
| BIC: Week 6 Post-partum (n=31) | 135058.9 (± 36348.21) | | | |
| BIC: Week 12 Post-partum (n=32) | 148265.3 (± 42201.47) | | | |
| FTC: Second Trimester (n=21) | 10258.5 (± 2049.53) | | | |
| FTC: Third Trimester (n=30) | 10434.2 (± 2121.13) | | | |
| FTC: Week 6 Post-partum (n=31) | 16329.7 (± 4095.44) | | | |
| FTC: Week 12 Post-partum (n=32) | 15308.5 (± 3359.79) | | | |
| TAF: Second Trimester (n=21) | 220.4 (± 98.98) | | | |
| TAF: Third Trimester (n=30) | 202.2 (± 84.98) | | | |
| TAF: Week 6 Post-partum (n=31) | 356.7 (± 151.27) | | | |
| TAF: Week 12 Post-partum (n=32) | 294.3 (± 97.88) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of BIC, FTC, and TAF

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|-----------------|--|
| End point title | PK Parameter: Cmax of BIC, FTC, and TAF ^[5] |
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End point description:

Cmax is defined as the maximum observed concentration of drug during the dosing interval. Participants in the PK analysis set with available data were analysed.

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| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

| End point values | B/F/TAF | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| BIC: Second Trimester (n=21) | 5819.0 (± 1752.29) | | | |
| BIC: Third Trimester (n=30) | 5374.7 (± 1393.86) | | | |
| BIC: Week 6 Post-partum (n=31) | 9765.5 (± 2274.93) | | | |
| BIC: Week 12 Post-partum (n=32) | 11025.3 (± 2747.42) | | | |
| FTC: Second Trimester (n=21) | 2639.1 (± 965.60) | | | |
| FTC: Third Trimester (n=30) | 2586.0 (± 686.42) | | | |
| FTC: Week 6 Post-partum (n=31) | 3394.8 (± 951.83) | | | |
| FTC: Week 12 Post-partum (n=32) | 3360.0 (± 902.47) | | | |
| TAF: Second Trimester (n=21) | 332.4 (± 173.29) | | | |
| TAF: Third Trimester (n=30) | 270.9 (± 113.93) | | | |
| TAF: Week 6 Post-partum (n=31) | 506.4 (± 249.33) | | | |
| TAF: Week 12 Post-partum (n=32) | 494.6 (± 259.51) | | | |

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| Attachments (see zip file) | Statistical Analysis/380- |
|----------------------------|---------------------------|

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Ctau of BIC and FTC

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|--|--|
| End point title | PK Parameter: Ctau of BIC and FTC ^[6] |
| End point description: Ctau is defined as the observed drug concentration at the end of the dosing interval. Participants in the PK analysis set with available data were analysed. | |
| End point type | Secondary |
| End point timeframe: Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum | |

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

| End point values | B/F/TAF | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| BIC: Second Trimester (n=20) | 1046.4 (± 472.68) | | | |
| BIC: Third Trimester (n=30) | 1072.4 (± 447.03) | | | |
| BIC: Week 6 Post-partum (n=31) | 3530.3 (± 1354.20) | | | |
| BIC: Week 12 Post-partum (n=32) | 3641.9 (± 1241.64) | | | |
| FTC: Second Trimester (n=21) | 59.8 (± 62.17) | | | |
| FTC: Third Trimester (n=30) | 51.4 (± 13.98) | | | |
| FTC: Week 6 Post-partum (n=31) | 152.1 (± 271.50) | | | |
| FTC: Week 12 Post-partum (n=32) | 81.1 (± 27.34) | | | |

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|-----------------------------------|---------------------------|
| Attachments (see zip file) | Statistical Analysis/380- |
|-----------------------------------|---------------------------|

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Clast of BIC, FTC, and TAF

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|--|---|
| End point title | PK Parameter: Clast of BIC, FTC, and TAF ^[7] |
| End point description: Clast is defined as the last observable concentration of drug. Participants in the PK analysis set with available data were analysed. | |
| End point type | Secondary |
| End point timeframe: Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum | |

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

| End point values | B/F/TAF | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| BIC: Second Trimester (n=21) | 1141.10 (± 631.431) | | | |
| BIC: Third Trimester (n=30) | 1075.13 (± 447.847) | | | |
| BIC: Week 6 Post-partum (n=31) | 3535.48 (± 1371.162) | | | |
| BIC: Week 12 Post-partum (n=32) | 3641.88 (± 1240.605) | | | |
| FTC: Second Trimester (n=21) | 75.08 (± 130.792) | | | |
| FTC: Third Trimester (n=30) | 51.65 (± 14.182) | | | |
| FTC: Week 6 Post-partum (n=31) | 156.16 (± 292.579) | | | |
| FTC: Week 12 Post-partum (n=32) | 81.18 (± 27.334) | | | |
| TAF: Second Trimester (n=21) | 4.49 (± 5.130) | | | |
| TAF: Third Trimester (n=30) | 4.80 (± 4.048) | | | |
| TAF: Week 6 Post-partum (n=31) | 3.13 (± 1.849) | | | |
| TAF: Week 12 Post-partum (n=32) | 3.36 (± 1.999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Tmax of BIC, FTC, and TAF

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|--|--|
| End point title | PK Parameter: Tmax of BIC, FTC, and TAF ^[8] |
| End point description: Tmax is defined as the time (observed time point) of Cmax. Participants in the PK analysis set with available data were analysed. | |
| End point type | Secondary |
| End point timeframe: Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum | |

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

| End point values | B/F/TAF | | | |
|---------------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| BIC: Second Trimester (n=21) | 2.00 (1.00 to 12.00) | | | |
| BIC: Third Trimester (n=30) | 2.00 (1.00 to 6.00) | | | |
| BIC: Week 6 Post-partum (n=31) | 1.50 (0.50 to 12.00) | | | |
| BIC: Week 12 Post-partum (n=32) | 1.50 (0.50 to 4.00) | | | |
| FTC: Second Trimester (n=21) | 1.50 (0.50 to 4.00) | | | |
| FTC: Third Trimester (n=30) | 1.50 (0.50 to 4.00) | | | |
| FTC: Week 6 Post-partum (n=31) | 1.50 (0.50 to 4.00) | | | |
| FTC: Week 12 Post-partum (n=32) | 1.00 (0.50 to 3.00) | | | |
| TAF: Second Trimester (n=21) | 0.75 (0.25 to 4.00) | | | |
| TAF: Third Trimester (n=30) | 1.00 (0.25 to 3.00) | | | |
| TAF: Week 6 Post-partum (n=31) | 0.75 (0.25 to 3.00) | | | |
| TAF: Week 12 Post-partum (n=32) | 0.75 (0.25 to 3.00) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: t_{1/2} of BIC, FTC, and TAF

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|-----------------|--|
| End point title | PK Parameter: t _{1/2} of BIC, FTC, and TAF ^[9] |
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End point description:

t_{1/2} is defined as the estimate of the terminal elimination half-life of the drug. Participants in the PK analysis set with available data were analysed.

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|----------------|-----------|
| End point type | Secondary |
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End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

| End point values | B/F/TAF | | | |
|---------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| BIC: Second Trimester (n=19) | 9.09 (4.75 to 16.04) | | | |
| BIC: Third Trimester (n=30) | 9.91 (7.53 to 16.24) | | | |
| BIC: Week 6 Post-partum (n=29) | 18.24 (12.18 to 29.59) | | | |
| BIC: Week 12 Post-partum (n=30) | 17.27 (4.534 to 26.3) | | | |
| FTC: Second Trimester (n=20) | 6.43 (4.76 to 7.36) | | | |
| FTC: Third Trimester (n=30) | 6.41 (4.49 to 7.91) | | | |
| FTC: Week 6 Post-partum (n=28) | 6.27 (4.47 to 7.80) | | | |
| FTC: Week 12 Post-partum (n=32) | 5.76 (3.83 to 8.19) | | | |
| TAF: Second Trimester (n=14) | 0.30 (0.22 to 0.66) | | | |
| TAF: Third Trimester (n=16) | 0.28 (0.19 to 0.62) | | | |
| TAF: Week 6 Post-partum (n=26) | 0.40 (0.25 to 0.60) | | | |
| TAF: Week 12 Post-partum (n=30) | 0.35 (0.25 to 0.60) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: CLss/F of BIC, FTC, and TAF

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|-----------------|---|
| End point title | PK Parameter: CLss/F of BIC, FTC, and TAF ^[10] |
|-----------------|---|

End point description:

CLss/F is defined as the apparent steady-state oral clearance following administration of the drug. Participants in the PK analysis set with available data were analysed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

| End point values | B/F/TAF | | | |
|--------------------------------------|------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: mL/h | | | | |
| arithmetic mean (standard deviation) | | | | |
| BIC: Second Trimester (n=20) | 911.78 (\pm 433.301) | | | |
| BIC: Third Trimester (n=30) | 902.47 (\pm 287.285) | | | |
| BIC: Week 6 Post-partum (n=31) | 399.02 (\pm 113.214) | | | |
| BIC: Week 12 Post-partum (n=32) | 362.40 (\pm 95.856) | | | |
| FTC: Second Trimester (n=21) | 20228.02 (\pm 3981.186) | | | |
| FTC: Third Trimester (n=30) | 19975.85 (\pm 4223.365) | | | |
| FTC: Week 6 Post-partum (n=31) | 12991.62 (\pm 3111.349) | | | |
| FTC: Week 12 Post-partum (n=32) | 13645.71 (\pm 2830.897) | | | |
| TAF: Second Trimester (n=15) | 122677.74 (\pm 44270.041) | | | |
| TAF: Third Trimester (n=17) | 135061.19 (\pm 44876.970) | | | |
| TAF: Week 6 Post-partum (n=27) | 76939.32 (\pm 29189.555) | | | |
| TAF: Week 12 Post-partum (n=30) | 92888.59 (\pm 29461.550) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Vz/F of BIC, FTC, and TAF

| | |
|-----------------|---|
| End point title | PK Parameter: Vz/F of BIC, FTC, and TAF ^[11] |
|-----------------|---|

End point description:

Vz/F is defined as the apparent volume of distribution of the drug. Participants in the PK analysis set with available data were analysed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

| End point values | B/F/TAF | | | |
|--------------------------------------|------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| BIC: Second Trimester (n=19) | 11896.24 (\pm 4417.149) | | | |
| BIC: Third Trimester (n=30) | 13406.77 (\pm 4349.429) | | | |
| BIC: Week 6 Post-partum (n=29) | 10348.47 (\pm 3713.380) | | | |
| BIC: Week 12 Post-partum (n=30) | 8692.59 (\pm 2398.645) | | | |
| FTC: Second Trimester (n=20) | 181767.32 (\pm 36739.344) | | | |
| FTC: Third Trimester (n=30) | 184791.79 (\pm 56340.526) | | | |
| FTC: Week 6 Post-partum (n=28) | 117384.90 (\pm 35385.941) | | | |
| FTC: Week 12 Post-partum (n=32) | 117660.87 (\pm 33240.095) | | | |
| TAF: Second Trimester (n=14) | 62333.17 (\pm 37242.307) | | | |
| TAF: Third Trimester (n=16) | 53230.98 (\pm 16727.325) | | | |
| TAF: Week 6 Post-partum (n=26) | 44440.06 (\pm 13678.515) | | | |
| TAF: Week 12 Post-partum (n=30) | 49837.70 (\pm 22019.454) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: λ_z of BIC, FTC, and TAF

| | |
|-----------------|--|
| End point title | PK Parameter: λ_z of BIC, FTC, and TAF ^[12] |
|-----------------|--|

End point description:

λ_z is defined as the terminal elimination rate constant, estimated by linear regression of the terminal elimination phase of the log plasma concentration of drug versus time curve of the drug. Participants in the PK analysis set with available data were analysed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

| End point values | B/F/TAF | | | |
|--------------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: 1/h | | | | |
| arithmetic mean (standard deviation) | | | | |
| BIC: Second Trimester (n=19) | 0.077 (± 0.0231) | | | |
| BIC: Third Trimester (n=30) | 0.068 (± 0.0125) | | | |
| BIC: Week 6 Post-partum (n=29) | 0.040 (± 0.0098) | | | |
| BIC: Week 12 Post-partum (n=30) | 0.043 (± 0.0134) | | | |
| FTC: Second Trimester (n=20) | 0.113 (± 0.0142) | | | |
| FTC: Third Trimester (n=30) | 0.112 (± 0.0173) | | | |
| FTC: Week 6 Post-partum (n=28) | 0.114 (± 0.0151) | | | |
| FTC: Week 12 Post-partum (n=32) | 0.120 (± 0.0209) | | | |
| TAF: Second Trimester (n=14) | 2.227 (± 0.7128) | | | |
| TAF: Third Trimester (n=16) | 2.550 (± 0.7519) | | | |
| TAF: Week 6 Post-partum (n=26) | 1.777 (± 0.4685) | | | |
| TAF: Week 12 Post-partum (n=30) | 1.954 (± 0.4519) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at the Time of Delivery Using the Missing = Excluded Approach in B/F/TAF Group

| | |
|-----------------|---|
| End point title | Percentage of Participants With HIV-1 RNA < 50 Copies/mL at the Time of Delivery Using the Missing = Excluded Approach in B/F/TAF Group ^[13] |
|-----------------|---|

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at the time of delivery was analysed in B/F/TAF group using missing = excluded approach. In this approach, all missing data were excluded in the computation of the percentages (ie, missing data points were excluded from both the numerator and denominator in the computation). Full analysis set included all adult participants who enrolled into the study and took at least 1 dose of study drug (B/F/TAF). Participants in the full analysis set with available data were analysed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At time of delivery

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This secondary endpoint was planned and analyzed only for the B/F/TAF group.

| End point values | B/F/TAF | | | |
|-----------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 100.0 (89.1 to 100.0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Birth Using the Missing = Excluded Approach in Neonates

| | |
|-----------------|---|
| End point title | Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Birth Using the Missing = Excluded Approach in Neonates ^[14] |
|-----------------|---|

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at the time of birth was analysed in neonates using missing = excluded approach. In this approach, all missing data were excluded in the computation of the percentages (ie, missing data points were excluded from both the numerator and denominator in the computation). Neonate full analysis set included neonates who were born to women participating in the study and had been enrolled into the study as well. Participants in the neonate full analysis set with available data were analysed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At birth

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This secondary endpoint was planned and analyzed only for the Neonates group.

| End point values | Neonates | | | |
|-----------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 100.0 (15.8 to 100.0) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality: From birth up to 8 weeks of age for neonates; From enrollment up to 38 weeks + 30 days for B/F/TAF group.

Adverse Events: First dose date up to 38 weeks + 30 days for B/F/TAF group

Adverse event reporting additional description:

B/F/TAF & Neonates: Safety analysis set. None of neonates participating in study were treated. Adverse events (AE) reported for that group are not treatment emergent (TE). TEAE: any AE with onset on/after start of study drug & no later than 30 days after permanent study drug discontinuation, or any AE leading to premature study drug discontinuation.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | B/F/TAF |
|-----------------------|---------|

Reporting group description:

Pregnant women participants received FDC tablet of B/F/TAF 50/200/25 mg, orally, once daily for up to 38 weeks (from the second or third trimesters of pregnancy, depending on enrollment, through 12 weeks post-partum).

| | |
|-----------------------|----------|
| Reporting group title | Neonates |
|-----------------------|----------|

Reporting group description:

Neonates born to women participants in the study were followed from birth up to 8 weeks of age after obtaining consent from the parent or legal guardian. None of the neonates participating in the study were treated with the study drug.

| Serious adverse events | B/F/TAF | Neonates | |
|---|-----------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 33 (18.18%) | 5 / 29 (17.24%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Congenital, familial and genetic disorders | | | |
| Accessory auricle | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial septal defect | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |

| | | | |
|--|----------------|----------------|--|
| Nonreassuring foetal heart rate pattern | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| False labour | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pre-eclampsia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Preterm premature rupture of membranes | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice neonatal | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Neonatal asphyxia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient tachypnoea of the newborn | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Covid-19 | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis neonatal | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | B/F/TAF | Neonates | |
|--|------------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 19 / 33 (57.58%) | 4 / 29 (13.79%) | |
| Cardiac disorders | | | |
| Foetal heart rate deceleration abnormality | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 29 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 29 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Headache | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 29 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Gestational diabetes | | | |
| subjects affected / exposed | 4 / 33 (12.12%) | 0 / 29 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Oligohydramnios | | | |

| | | | |
|---|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 33 (6.06%) 2 | 0 / 29 (0.00%) 0 | |
| Postpartum haemorrhage subjects affected / exposed occurrences (all) | 2 / 33 (6.06%) 2 | 0 / 29 (0.00%) 0 | |
| Pre-eclampsia subjects affected / exposed occurrences (all) | 2 / 33 (6.06%) 2 | 0 / 29 (0.00%) 0 | |
| Jaundice neonatal subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 2 / 29 (6.90%) 2 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 3 / 33 (9.09%) 3 | 0 / 29 (0.00%) 0 | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 2 / 33 (6.06%) 2 | 0 / 29 (0.00%) 0 | |
| Haemorrhoids subjects affected / exposed occurrences (all) | 2 / 33 (6.06%) 2 | 0 / 29 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders Respiratory distress subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 3 / 29 (10.34%) 3 | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 4 / 33 (12.12%) 4 | 0 / 29 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported